FOOD AND DRUG ADMINISTRATION

CENTER FOR BIOLOGICS EVALUATION AND RESEARCH

MEMORANDUM

DATE: September 23, 1998

FROM: J. Lloyd Johnson, Pharm.D., DMPQ, HFM-206

THRU: Julia Lukas Gorman, Chief, Branch I, DMPQ, HFM-206

SUBJECT: Review of Genentech's rhuMAb HER2, BLA Ref. No. 98-0369; CMC section Volume 7, Facilities and establishment descriptions

TO: Keith Webber, Ph.D., DARP, OTRR, HFM-594

Trastuzumab (Herceptin®) is a recombinant DNA-derived humanized monoclonal IgG_1 antibody produced in mammalian cell culture using Chinese hamster ovary(CHO)cells. The antibody selectively targets the human epidermal growth factor receptor 2 protein (HER-2) that is overexpressed in breast cancer cells.

Drug Product:
Trastuzumab is provided as a lyophilized protein, each vial contains 440 mg Trastuzumab, 9.9 mg L-histidine HCL, 6.4 mg L-histidine, 400 mg trehalose dihydrate, and 1.8 mg polysorbate 20. Each vial configuration is designed to deliver ——— of trastuzumab per vial. Herceptin is reconstituted with 20 ml Bacteristatic Water For Injection (BWI), containing 1.1 % benzyl alcohol.

BWI is commercially available and is supplied by ——— Additional stability data for the BWI diluent which supports actual shelf life claim for the product was submitted.

Genentech, Inc., South San Francisco is responsible for the manufacture, testing and release of the trastuzumab drug substance (Bulk for Storage) and drug product.

——— is listed an alternate contract testing facility for Sterility testing of Trastuzumab Sterile filtered bulk.

Trastuzumab is manufactured at Genentech's licensed multi-product facility. The CMC section of the BLA (Vol. 7: Methods of Manufacturing, Buildings and Facilities descriptions) of this application describes or provides sufficient information and adequately addresses multi-product facility control issues and concerns with respect to product campaigning, product changeover, segregation procedures, cleaning validation, cross contamination precautions and testing.

Product flow as well as the flow of equipment and materials appear to be well designed for Bldg. 3A/3B (cell culture production). The general descriptions provided in the CMC section with regard to validation of major systems and equipment appear to be complete and well documented.

Validation data for major systems and equipment, process controls, operating procedures, documentation and records were reviewed and or verified during the pre-approval inspection to assess the firm's capability to manufacture under cGMP condition. The pre-approval inspection of the Genentech's manufacturing facilities for this product was completed in June of 1998 by Mr. Walt Lange and Dr. Julia Goldstein of CBER and Raymond Oji from SFDO.

THIS PAGE WAS DETERMINED TO BE NOT RESPONSIVE TO YOUR REQUEST

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